

Amendments to the Claims

Claim 1 (Currently amended): A method for producing viral vectors in a ~~establishing a~~
~~vector packaging cell line with favorable vector packaging efficiency~~ comprising:
transducing a packaging cell line with a viral vector comprising a packaging sequence and a gene
of interest;
introducing a helper virus ~~into a cell to establish a packaging cell line~~, said helper virus
comprising retroviral structural genes in combination with an internal ribosome entry site
linked to a selection marker; ~~and~~
~~eliminating cells with methylated helper virus thereby increasing virion production~~
selecting for helper virus containing cells in which the helper virus DNA is not
methylated by growing the cells in the presence of a selection agent thereby increasing
virion production.

Claim 2 (Previously amended): The method of claim 1 wherein said step of ~~eliminating~~
selecting cells not ~~with methylated helper virus~~ comprises:
positively selecting helper virus which is functional.

Claim 3 (Original): The method of claim 2 wherein said selection is by antibiotic resistance.

Claim 4 (Original): The method of claim 3 wherein said antibiotic resistance selection ~~is~~
~~accomplished via ligation of an internal ribosome entry site with a selection marker so that drug~~
~~selection~~ ensures promoter function in said helper virus.

Claim 5 (Original): The method of claim 1 wherein said viral titer achieves levels of 1.5×10^7 cfu/ml in the presence of antibiotic resistant selection.

Claim 6 (Original): The method of claim 1 wherein said helper virus comprises at least one viral production gene operably linked to viral promoter sequence which is capable of being methylated.

Claim 7 (Original): The method of claim 6 wherein said viral promoter comprises a long terminal repeat.

Claim 8 (Currently amended): The method of claim 7 wherein said viral promoter sequence is the long terminal repeat ~~LTR~~ of a retrovirus.

Claim 9 (Currently amended): The method of claim ~~3~~ 1 wherein said ~~selection eliminates cells with~~ growing cells in the presence of the selection agent positively selects for cells in which the methylated 5' long terminal repeat of the helper virus is not methylated ~~LTR~~.

Claim 10 (Previously amended): The method of claim 1 wherein said selecting for helper virus DNA not methylated ~~eliminating methylation~~ is accomplished by treating vector producer cells with 5-AZA-C.

Claims 11-13 (Withdrawn)

Claim 14 (Cancelled)

Claims 15-25 (Withdrawn)

Claim 26 (Currently amended): A method for producing viral particles ~~increasing the presence of viral titer~~ produced by a vector packaging cell upon transfection with a viral vector comprising:

introducing into a packaging cell line a viral vector comprising a packaging sequence and a gene of interest;

transfecting the packaging cell line with a helper virus comprising retroviral structural genes in combination with an internal ribosome entry site linked to a selection marker;

selecting for non-methylated helper virus-containing cells thereby decreasing the amount of inactive helper virus present in said vector packaging cell ~~by providing for the elimination of or prevention of methylated helper virus.~~

Claim 27 (Previously amended): A method of claim 26 wherein said step of ~~decreasing~~ selecting for non-methylated ~~inactive~~ helper virus comprises ~~the step of:~~ selecting for functional ~~eliminating methylation of~~ helper virus.

Claim 28 (Currently amended): The method of claim 26 wherein said step of decreasing inactive helper virus comprises the steps of:

removing from a population of vector packaging cells, helper virus with 5' long terminal repeat methylation.

Claim 29 (Currently amended): The method of claim 28 further comprising the steps of:
removing cells with inactivated virus by positive selection.

Claim 30 (Currently amended): The method of claim 29 wherein said removal step comprises:
introducing an antibiotic ~~to~~ to said cells so that cells with inactive helper virus are killed.

Claim 31 (Original): The method of claim 30 wherein said removal is accomplished by a helper virus with a picarnovirus internal ribosomal entry site sequence followed by an antibiotic resistance marker at the 3' end of the env sequence of said helper virus.

Claim 32 (Original): The method of claim 31 wherein said antibiotic resistance selection marker is Zeocin.

Claim 33 (Original): The method of claim 27 wherein said inhibiting of methylation is selection is accomplished by a step selected from the group consisting of:
treating ~~of~~ vector producer cells with 5-ACA-C.

Claim 34 (Withdrawn)

Claim 35 (Previously amended): The method of claim ~~27~~ 26 wherein said reducing the presence inhibiting of methylated helper virus methylation is accomplished by a step selected from the group consisting of:

ligation of an internal ribosome entry site with a selection marker so that drug selection would ensure promoter function.